Reply to 'Is single portal vein perfusion the best approach for machine preservation of liver grafts?'

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Reply to „ Is single portal vein perfusion the best approach for machine preservation of liver grafts? “

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To the Editor:

We appreciate the interest and comments expressed in the letter by Isabel et al. concerning our recent findings on single portal vein hypothermic liver graft perfusion prior to transplantation (1).

The authors argue that single portal vein perfusion in the cold may not be sufficient for preservation of the extrahepatic bile duct of liver grafts, in contrast to dual HOPE (portal vein plus hepatic artery). This statement is based on the fact, that our images lack information on histological scoring of the perivascular biliary plexus. The authors claim also direct measurement of oxygen saturation and ATP analysis of the bile duct wall during single portal vein perfusion. In addition, they refer to publications from 2003 and 1999 on the effects of dual (hepatic artery and portal vein) perfusion on biliary secretion (2,3).

We agree that ATP measurements in bile duct tissue could in theory further support the presence of oxygen for aerobic metabolism in biliary epithelial during single portal vein perfusion. We showed, however, that the extrahepatic bile duct wall in both rodent and human DCD liver grafts is completely stained with a perfusate containing fluoresceine and also oxygen (60-80 kPa) (4). Based on this, our study demonstrated that HOPE through the portal vein transports perfusate, loaded with a high amount of oxygen, to the entire extrahepatic bile duct.

To underline viability of the extrahepatic Choledochus after reperfusion, we provide detailed histological images and scoring of human DCD bile ducts after portal vein HOPE treatment and transplantation. Supporting an intact biliary epithelium, we failed to document any mural necrosis, vascular injury, or even deep peribiliary gland injury, and the absence of inflammation (Figure 1) (5).

Under normothermic perfusion conditions, as stated in the studies by Foley et al, dual blood perfusion supply is essential for biliary function and epithelial viability (2, 3). The hypothermic perfusion setting, however, fundamentally differs from normothermic physiological conditions. During cold machine liver perfusion, oxygen consumption of any liver cells, including the extrahepatic bile duct, is dramatically reduced, and we convincingly reported that single portal vein perfusion with high oxygen tension enables sufficient liver ATP reload in the cold before graft implantation (6-8).To support our observation, recent human application of single

portal vein HOPE in extended DCD livers displayed a significant reduction of biliary complications with robust graft survival benefit, compared to matched unperfused DCD livers (9).

In summary, we believe that single portal vein HOPE is very effective. It is currently the simplest machine perfusion approach, with therefore high practicability and low associated costs. We agree that randomized trials remain needed to identify the best liver perfusion strategy, but, it is rather unlikely that additional arterial perfusion during HOPE in the cold would add more oxygen availability to the intra- and extrahepatic biliary tract, and thereby to be of any benefits.

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Figure legend

Figure 1: Extrahepatic bile duct of human DCD liver graft after single portal vein HOPE and transplantation (* luminal surface). The mural stroma of the bile duct wall is healthy without necrosis (A, B) (#).Higher magnification displayed no loss of epithelial cells in periluminal peribiliary glands (arrows)(C,D), and also normal appearance of deep peribiliary glands (arrows)(E,F). The peribiliary vascular plexus shows normal vascular structure (G).